

Olfactory Functioning and Callosotomy: A Report of Two Cases

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Two callosotomy patients with presumably intact anterior commissures were evaluated on a battery of olfactory tasks including sensitivity, discrimination, memory, identification, cross-modality matching, bilateral summation (dirhnic vs. monorhnic thresholds), and localization of odorants. One case was evaluated both pre- and post-surgery. He showed marked decrements after surgery in odor memory and in matching across modalities. After surgery, both patients were better able to name odorants presented to the left nostril than the right nostril. The patient who was asked to remember odorants that could be readily labeled was better able to remember those odorants presented to the left nostril. The findings that both cases performed equally well whether olfactory and tactile information was projected to the same hemisphere or a different one, that some bilateral summation was evident, and that the cases were unable to localize odorants suggests that the remaining neuronal pathways allow for some communication between hemispheres.

INTRODUCTION

When the human brain is divided by surgical section of the cerebral commissures, the functional communication between the hemispheres breaks down so that information which is presented to the one hemisphere may not be comprehended entirely by the other [1]. Studies on patients who have undergone bisection of the cerebral hemispheres for relief of intractable epilepsy indicate that the disconnected left "dominant" hemisphere is more likely to understand and produce language, whereas the right "nondominant" hemisphere may mediate visuospatial functions [2]. Previous studies in patients with commissurotomy have examined the transmission of olfactory information between the hemispheres and the capacity of each hemisphere to comprehend such information [3-6]. These reports have focused on the ability of these patients to name odorants or to select the objects, visually or tactually presented, that corresponded to the odorants.

Preservation of olfactory processing seems to depend on the extent and nature of the bisection. Patients with complete commissurotomy generally were unable to name odors presented to the right nostril (right hemisphere) and sometimes denied the presence of odor in that nostril [3-5]. These patients could, however, correctly point to

Abbreviation: DDS: double simultaneous stimulus

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a matching object. If the matching objects were tactually presented, the patients performed better when the olfactory and tactile stimuli projected to the same hemisphere. A patient with an intact splenium but with bisection of the anterior commissure and two-thirds of the callosum could identify some odorants presented to the right nostril, though he identified more of those presented to the left [3]. On an odor-tactile task, the patient performed equally well for all nostril-hand combinations. Similarly, patients with callosotomies but with intact anterior commissures could identify odorants presented to the right nostril, although three out of the four patients reported in the literature identified more odorants presented to the left nostril [5,6].

The present study provides a description of olfactory functioning in two callosotomy patients with intact anterior commissures on a wider variety of tasks than those previously used. We hoped to address a number of questions:

1. Do callosotomy patients with presumably intact anterior commissures demonstrate differences in the olfactory functioning of their right and of their left nostrils? Specifically, can they detect, discriminate, identify, and remember odorants equally well regardless of which nostril sniffs? Can they match odorants to objects presented visually or tactilely even when information is presented to opposite hemispheres?
2. Are the findings of deficits in olfactory functioning previously reported in the literature reflective of pre-surgical deficits? Does performance return to pre-surgery functioning with time? We report olfactory functioning in one callosotomy patient, S.F., both pre-surgery and three and seven months post-surgery.
3. Do callosotomy patients who have intact anterior commissures show bilateral summation of odors? Previous psychophysical studies have suggested bilateral additivity of odor intensity in normal participants [7].
4. Are those with callosotomy at an advantage for localization (lateralization) of odors? A pilot investigation in our laboratory indicated that the experimenters could not localize which nostril received olfactory stimulation. On the assumption that failure to localize derives from the bilateral integration of olfactory information in the intact brain, it seemed worthwhile to explore whether persons with bisected brains might be able to tell which nostril was stimulated.
5. With a double simultaneous stimulation paradigm, would callosotomy patients demonstrate response bias to the left or right nostril? One of our callosotomy patients showed a mild unilateral inattention of the left space. Since a right-sided lesion usually underlies a left inattention, sensory theories [8,9] would predict that olfactory information which projects to the right hemisphere (right nostril) would be impaired. On the other hand, the more accepted representational theories suggest that a right (usually parietal) lesion produces a distorted body schema with an inattention of all information on the left side of space and thus would predict impaired performance via the left nostril [10,11].

METHODS

Cases S.F. and M.D.

Two patients who had received callosotomy at Yale-New Haven Hospital participated. S.F., a white 20-year-old male, was reported to have had his first seizure, involving the tonic stiffening of his arms, at age eight followed one month later by an akinetic seizure. Episodes of status epilepticus with generalized convulsions occurred

several times per year throughout his teens. Pneumoencephalogram showed a slight dilation of the right lateral ventricle, but cerebral angiography and CT scans were normal. Interictal scalp EEG demonstrated predominantly right but also left frontal shape waves, spike and waves, and polyspike and waves. Depth electrode EEG revealed evidence of right temporal or frontal seizure onset, although left temporal discharges were also commonly observed. No primary lesion site was identified. The etiology of his seizures was unknown.

M.D., a white 21-year-old male, displayed episodic staring at bright objects and lights as early as 18 months and, by the age of 18, the seizures, consisting of impairment of consciousness and falling, occurred as often as ten times a day. Ventriculogram demonstrated dilation of the right occipital horn, and CT scan revealed right posterior atrophy. Depth electrode EEG study demonstrated interictal discharges from the right posterior and right and left frontal areas. No single seizure focus could be identified. No specific etiology could be determined.

Both M.D. and S.F. possessed low normal intelligence quotients (WAIS Full-Scale IQ = 83 and 82, respectively) at the time of testing, had twelfth grade educations, and were right-hand dominant. Neither smoked nor had allergies.

Both cases had received surgery for their intractable epilepsy. Surgery consisted of retraction of the nondominant right hemisphere and entry into the roof of the lateral ventricle. Section of the inferior callosal remnants was performed under microsurgery. The massa intermedia was not sectioned. The anterior commissure was not visualized in either patient during surgery and presumably remained intact.

M.D. underwent surgery twice, first for bisection of the anterior three-quarters of the callosum and, four months later, for bisection of the remaining callosum when his seizures had not improved. After the second procedure, M.D. demonstrated a profound reduction in the severity of seizures. At the time of olfactory testing, six months later, he still had seizures which were either absence-like seizures lasting two to three seconds or left-body focal motor seizures with impairment of consciousness without falling.

S.F., who received complete callosotomy in a single operation, initially showed some abatement of his seizures. In the ensuing three years, however, the severity of his seizures returned to the pre-surgery level. He exhibited generally tonic-clonic seizures. Since surgery, S.F. has shown a mild left heminattention with some dyspraxia of the left arm and leg.

We evaluated S.F. two weeks prior to surgery and three and seven months after surgery. M.D. was tested six and nine months post-surgery.

Procedure

Table 1 provides an outline of tasks and the schedule of administration. Most of the tasks were administered to both callosotomy patients. The odorants were administered to one nostril (monorhinally), while the other nostril was held closed either by the experimenter or the subject. Approximately 15 seconds were allowed between trials. All testing was done in well-ventilated rooms. S.F. was evaluated on all but one task both pre- and post-surgery. The tasks included:

1. *Threshold sensitivity with mono- and dirhinic (one- and two-nostril) presentation:* Threshold determination followed a two-alternative, forced-choice procedure with concentration increasing from low to high until the patient achieved a criterion of four successive correct choices [12]. The lowest concentration equalled 10^{-6} (in three

TABLE 1
Schedule of Test Administration

	Case S.F.			Case M.D. Post-Surgery	
	Pre-Surgery	Post-Surgery		6 months	9 months
		3 months	7 months		
1. Threshold					
Monorhinic	x	x	x	x	x
Dirhinic	—	—	x	x	x
2. Discrimination	x	x	—	—	—
3. Recognition memory					
Test 1	x	x	—	—	—
Test 2	—	—	—	x	—
4. Identification	x	x	x	x	—
5. Odor-visual	x	x	—	—	—
6. Odor-tactile	x	x	—	—	x
7. Localization	—	—	x	—	x

sessions) or 10^{-5} M (in two sessions). On each trial, the patient was presented with two bottles, one containing a weak solution of 1-butanol and the other, distilled water. The patient sniffed each bottle consecutively via one nostril and indicated which bottle “smelled stronger.” Sensitivity was determined for each nostril separately. Sensitivity was also determined for both nostrils together by presenting simultaneously two bottles of butanol (one to each nostril) or two of water.

2. Odor discrimination: On each trial, S.F. was asked to sniff the odorants from three vials presented in random order. The odorants were dripped onto a cotton ball and placed in a small glass vial. Two vials contained the same and one a different odorant. S.F. sought to choose which two smelled the same. The three odorants were presented to the same nostril on a given trial while the other nostril was held closed. In pre-surgery testing, the odorants were benzyl acetate, geraniol, methyl butyrate, benzaldehyde, and pyridine. In post-surgery testing, the odorants were l-carvone, ethyl-*n*-butylamine, pentanedione, benzaldehyde, and pyridine. S.F. was instructed to remember the odorants for a subsequent test of odor recognition memory. The pure chemicals selected for this task were chosen because they were not readily identified verbally and, therefore, S.F. was less likely to remember an odorant by its label. There were 40 trials, 20 per nostril.

3. Recognition memory: S.F. and M.D. were evaluated on different recognition memory tasks. On each of 20 trials (ten per nostril), S.F. was presented with two vials of odorants to one of his nostrils, one from the discrimination task (above) and the other a new distractor. He was asked to decide which odorant he had smelled on the immediately preceding task. Each “old” odorant was presented to each nostril. On the pre-surgical testing, five different distractors were used. Because we thought that repeated use of the same distractors may have confused the participant about the “old” and “new” odorants on the pre-surgical testing, we selected a different distractor for each trial (20 distractors) on the post-surgical testing. We hypothesized that this change in method would serve to reduce the difference between pre- and post-surgical testing.

M.D. sniffed 14 everyday odorants (targets) such as chocolate, shoe polish, crayons, and garlic, presented in random order. The odorants were presented in opaque jars, covered with gauze. Presentation alternated from one nostril to the other on successive trials, so that each nostril was presented with seven odorants. After a delay of ten minutes and again after a delay of 40 minutes, the 14 targets were randomly interspersed with 14 distractor odorants. Different distractors were used at the ten-minute and at the 40-minute delays. M.D. decided which were the "old" (target) and which were the "new" (distractor) odors. Target odorants were always presented to the same nostril. No odorants were presented during the delay.

4. *Odor identification:* In this task, the patients referred to an alphabetical list of 20 odorant names in order to identify ten odorants. The list contained the names of the ten test items (baby powder, chewing gum, chocolate, cinnamon, coffee, mothballs, peanut butter, potato chips, soap, and wintergreen) and ten distractor names (burnt paper, garlic, ketchup, black pepper, rubber, sardines, spoiled meat, tobacco, turpentine, and wood shavings). On a trial, the patient was given an opaque plastic jar, covered with gauze, containing the odorant. With his eyes closed, he smelled the odorant through one nostril. He then matched the smell to its name on the list. He received corrective feedback if incorrect. Each odorant was presented six times monorhinally, three times to each nostril, for a total of 60 trials.

5. *Odor-visual matching:* This task was administered only to S.F. The task entailed random presentation of 15 common everyday odorants in opaque plastic jars: Band-aid, garlic, bubble gum, popcorn, coconut, mustard, crayon, cigarette, black pepper, pencil, orange, apple, pipe tobacco, cherry, and olive. S.F. sat in front of an array of the 15 corresponding stimulus objects and pointed to the object that matched the smell. If he chose incorrectly, we pointed to the correct object. For pre-surgery testing, each odorant was presented only twice, once to each nostril (30 trials). He used the right hand to point to the corresponding object. In post-surgery testing, each odorant was presented four times, once for each hand-nostril combination (60 trials).

6. *Odor-tactile matching:* After blindfolding the patient, we guided his hand to each of ten objects in an array. He was asked to explore each one tactually. The objects included a bar of soap, a block of wood, an onion, a newspaper, peanuts, a tea bag, a banana, a piece of rubber hose, an egg, and a lemon. We then presented an odorant (in an opaque jar) to one of his nostrils. The patient was asked to find the object that matched the odor. If incorrect, his hand was guided to the appropriate object. Each odorant was presented once per nostril-hand combination (40 trials, ten trials per combination). At the end of each test session, the patient named the objects while he was still blindfolded. In addition, M.D. was asked to match test objects to the same objects in the array by palpation (tactile-tactile match).

7. *Odor localization (lateralization):* After a number of trials to familiarize the patient with the odors, benzaldehyde (almond odor) was presented to one nostril while the odorless diluent diethyl phalate (20 trials) or linalool (citrus) (40 trials) was simultaneously presented to the other. He sought to determine which nostril received the benzaldehyde, which was presented an equal number of times to each nostril. This task was repeated, using linalool as the target and either diluent or benzaldehyde as the distractor (20 trials). The participant was asked to respond while sniffing (inhaling) the odorant to avoid cross-nostril stimulation.

TABLE 2
Threshold Sensitivity for Monorhnic and Dirhnic Stimulation^a

	Case S.F.			Case M.D.		Normal Controls <i>n</i> = 17 ^b
	Pre-Surgery	Post-Surgery		Post-Surgery		
		3 months	7 months	6 months	9 months	
Right nostril	7.5	7.5	7.5	4.0	8.0	7.5
Left nostril	9.0	7.5	11.0	7.0	8.5	7.5
Dirhinic	—	—	12.0	7.5	9.5	7.6

^aThe numbers represent log₃ dilution from a 4 percent solution; hence, the higher the number, the more sensitive the subject.

^bBased on a group of normal controls who are slightly older (*m* = 34 years) and more educated (*m* = 13.4 years) than the callosotomy patients

RESULTS AND DISCUSSION

Right vs. Left Nostril Post-Surgery

In response to question 1 in the Introduction, S.F. and M.D. showed some differences between right and left nostrils after callosotomy surgery. They both had clinically normal thresholds with inconsistently better sensitivity in the left nostril (refer to Table 2). As shown in Table 3, S.F. showed a left nostril advantage in odor discrimination, with performance via the right nostril below chance level. Difference in thresholds could in part explain the disparity between nostrils; however, threshold would not explain the chance performance in odor discrimination via the right nostril, since the threshold in this nostril was within normal limits.

Both S.F. and M.D. were better able to identify odors presented to the left nostril.

TABLE 3
Post-Surgical Differences Between Right and Left Nostrils^a

	Chance Probability (%)	Case S.F. % Correct		Case M.D. % Correct		Normal Controls
		Right Nostril	Left Nostril	Right Nostril	Left Nostril	% Correct Mean ± S.D.
Discrimination	33	25	45	—	—	87.3 ± 9.5 ^c
Recognition memory ^b						
Immediate	50	30	30			96.3 ± 8.5 ^c
Delayed	50			71	86	69 ± 15 (R) 76 ± 15 (L) ^d
Identification	5	50	70	57	79	75 ± 11 (R) 74 ± 11 (L) ^d
Odor-visual matching	7	43	40	—	—	89.6 ± 10.3 ^c
Odor-tactile matching	10	45	35	40	35	88.9 ± 10.2 ^c
						88.5 ± 11.4 ^c

^aEntries assume that probability remains the same throughout a test.

^bDifferent tests were administered to S.F. and M.D.

^cTasks were different only in that the stimuli were presented dirhinally to normal controls (*n* = 46). Controls were slightly older (*m* ± SD = 33 ± 9.2 years) and more educated (*m* ± SD = 13.8 ± 2.3 years) [13].

^dMonorhinal presentation to normal controls (*n* = 17) with a mean age of 33.5 years and education of 13.5 years [14]

TABLE 4
Pre-Surgical and Post-Surgical Performance of Case S.F.

	Pre-Surgery % Correct	Post-Surgery % Correct	
		3 months	7 months
Discrimination			
Right nostril	50	25	—
Left nostril	40	45	—
Recognition memory			
Right nostril	60	30	—
Left nostril	50	30	—
Identification			
Right nostril	30 (60) ^a	50 (33) ^a	50 (57) ^a
Left nostril	50 (73)	70 (60)	70 (63)
Odor-visual matching			
Right nostril	64	43 (53) ^b	—
Left nostril	57	40 (53) ^b	—
Odor-tactile matching			
Right nostril	60	45	—
Left nostril	45	35	—

^aThe values in parentheses represent performance over all three trials with the benefit of corrective feedback; the values preceding the parentheses represent performance in the first trial only (i.e., initial identification).

^bThe numbers preceding the parentheses represent performance across all trials; the numbers inside the parentheses represent performance when pointing with the right hand only. For pre-surgery evaluation, only the right hand was used.

S.F., who was required to remember odorants which were relatively difficult to label, remembered an equal number of odorants via the right and left nostrils but performed worse than chance. To some extent his inability to remember odorants was probably due to his initial difficulty in learning to discriminate them, particularly those presented via the right nostril. On a task where odorants could be easily labeled, M.D. remembered more odors presented through the left nostril and performed above chance level. The disparity between nostrils was even greater at the 40-minute delay.

In contrast, performance on the cross-modality tests, such as odor-tactile and odor-visual matching, demonstrated no clear nostril advantage. Neither S.F. nor M.D. matched more odorants to objects when tactile and olfactory information projected to the same hemisphere (right hand-right nostril or left hand-left nostril = 35 percent for M.D. and 40 percent for S.F. versus right hand-left nostril or left hand-right nostril = 40 percent for M.D. and 40 percent for S.F.). McKeever et al. [13] demonstrated that patients with callosotomy but with presumably intact anterior commissures demonstrate deficits in interhemispheric transfer of tactile information. This disability was measured not by odor-tactile matching, as in our study, but by the number of objects that they could name when presented to the nondominant hand. It is yet unclear whether the anterior commissure or some other subcortical pathway, as suggested most recently [14], provides for the interhemispheric communication that we observe.

Pre-Surgery vs. Post-Surgery Performance

Question 2 asks whether deficits in olfactory functioning following callosotomy are present even before surgery. Table 4 shows that some of the differences between right

and left nostrils which S.F. demonstrated existed even before surgery. He identified fewer odorants via the right nostril but showed a right nostril advantage in odor-tactile matching.

S.F.'s ability to discriminate, to remember odorants, and to match odorants to objects visually or tactually presented declined with surgery. He could identify more odorants post-surgery than pre-surgery, with no further improvement after three months post-surgery. S.F., however, learned fewer labels for odorants (with corrective feedback) after surgery, particularly when the odorant was presented to the right nostril. The ability to learn labels for odorants presented via the right nostril returned to pre-surgical levels by seven months post-surgery.

We note that, overall, S.F.'s performance on all the tests of olfactory functioning both pre- and post-surgery was considerably worse than performance on similar tasks (but administered dirhinically) of patients who had undergone temporal lobectomy surgery for intractable epilepsy [15]. The only exception to this statement was that S.F. could identify odorants as well as lobectomy patients post-surgery. M.D., on the other hand, performed comparably to lobectomy patients on similar tasks and, at times, as well as normal controls [16]. Other investigators have reported that commissurotomy patients are impaired on visuospatial and verbal memory, especially in the first year following surgery [17] and that commissurotomy patients may be more impaired than temporal lobe epileptics and lobectomy patients [18]. On memory for relatively nonverbalizable odorants, S.F., three months post-surgery, performed much worse than normal controls and lobectomy patients but, on memory for readily labeled odorants, M.D., six months post-surgery, remembered as many odorants as normal controls and lobectomy patients. It is possible that olfactory memory may recover more rapidly than visuospatial or verbal memory.

Bilateral Summation

In answer to question 3, S.F. and M.D. demonstrated some evidence of bilateral summation. Dirhinic presentation of butyl alcohol revealed that more dilute concentrations could be detected with both nostrils sniffing simultaneously better than with either nostril alone (refer to Table 2). This finding could be interpreted as bilateral summation, an outcome previously seen but insufficiently explored for olfaction [7]. For the same task, normal controls, on average, exhibited only slightly better sensitivity for dirhinic stimulation than monorhinic.

Localization (Lateralization)

For the localization (or, more precisely, lateralization) task presented here, we had no normative data, but we found that the experimenters could not perform above chance (50 percent). We expected that a separation of the hemispheres may aid in the localization of odorants and that the patients would perform better than we did; however, the callosotomy patients also performed around the 50 percent chance level (S.F., 48 percent correct; M.D., 55 percent correct).

Response Bias

We queried in question 5 whether a callosotomy patient who demonstrated unilateral inattention of the left space would also demonstrate "neglect" of the left nostril or a response bias to the right. Other investigators who did not employ a double simultaneous stimulus (DSS) paradigm have reported that patients with complete

commissurotomy tend to deny smelling in the right nostril when a verbal response is required [3–5]. Although on similar tasks our callosotomy patients did not deny smelling via the right nostril, they did perform slightly more poorly via the right nostril. In contrast, on the localization task which employs a DSS paradigm, we found that S.F. displayed a strong response bias to the right which explains his poor performance via the left nostril (S.F.: right, 68 percent correct; left, 25 percent correct). He perceived the target odorant to be in the right nostril 71 percent of the time, whereas M.D. perceived it to be on the right only 51 percent of the time.

S.F. had shown a mild inattention to the left space on other tasks; for example, when asked to draw a clock and a daisy, S.F. neglected to draw the left half. Mesulum [19] described a hemineglect patient who neglected the left nostril. Recent research in our laboratory on stroke patients who demonstrate left inattention on tactile DSS tasks also shows left inattention on an olfactory DDS task [20]. Inattention of the left nostril supports the body schema or representational theories of neglect.

CONCLUSIONS

Our study confirms previous findings [5,6] which showed callosotomy patients with presumably intact anterior commissures to have a better ability to name odorants presented to the left nostril. The pre-surgery evaluation of S.F. revealed, however, that this disparity existed even prior to surgery. The only other nostril difference was found in M.D., who demonstrated a left nostril advantage in remembering odorants which could be readily labeled, especially over the longer delay (40 minutes). We do not know whether this disparity existed prior to surgery. A comparison of pre-surgical and post-surgical performance of S.F. revealed a marked decrement in his ability to remember odorants and to match across modalities. Future studies of patients who undergo brain bisection should include pre-surgery evaluation in order to determine the actual effects of the surgery.

Our study also suggests that the anterior commissure or subcortical pathways allow for some communication between hemispheres. Both patients performed equally well whether olfactory and tactile information projected to the same hemisphere or to different hemispheres. The pathways that remain intact are sufficient to allow for information to transfer for bilateral summation and for interference in localization of odorants. Further investigation should include comparison of callosotomy patients with intact anterior commissures and those without.

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